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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/761,636 | 01/21/2004 | Bernard Frank Bishop | PC22004B | 3343 |

25533 7590 12/28/2006

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| EXAMINER | |
|---|---|
| MCINTOSH III, TRAVISS C | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 12/28/2006 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/761,636 | BISHOP, BERNARD FRANK | |
| | Examiner | Art Unit | |
| | Traviss C. McIntosh | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,4,6-8 and 10-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6-8 and 10-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/15/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 9/15/2006 has been entered.

An action on the merits of claims 1, 3-4, 6-8, and 10-19 is contained herein below.

In an effort to make the record clear, it is noted that the below 112 1st paragraph rejection is being set forth again, as drawn to the rejection of claims in the office action mailed on 2/8/2006. The examiner amended claim 13 in the examiner's amendment mailed on 5/9/2006, which obviated the rejection, however, to ensure the claims are amended, the examiner is setting forth the rejection again and respectfully request applicants to provide the claims as amended in response to this action, to ensure there is no confusion regarding the status/substance of the claims. Moreover, it is noted that claim 19 is being added to the rejection, and therefor requires amending also.

### *Claim Rejections - 35 USC § 112*

Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment and prevention of flea and heartworm infections, and for

treatment of tapeworm infections using praziquantel and selamectin, does not reasonably provide enablement for prevention of tapeworm. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

**The breadth of the claims - The nature of the invention**

Claim 13 of the instant application is drawn to a method for preventing and treating flea, heartworm, and tapeworm infections using praziquantel and selamectin. Claims 14-17 provide various dosing regiments and claim 18 provides the method is to be practiced on a cat. Claim 19 is drawn to a kit comprising a composition used for the same purposes as the method claimed.

**The state of the prior art**

Selamectin is known in the art to: "...kills adult fleas and prevents flea eggs from hatching for one month and is indicated for the prevention and control of flea infestations (Ctenocephalides felis), prevention of heartworm disease caused by Dirofilaria immitis, and the treatment and control of ear mite (Otodectes cynotis) infestations in cats and dogs. Revolution also is indicated for the treatment and control of sarcoptic mange (Sarcoptes scabiei) and for the control of tick (Dermacentor variabilis) infestations in dogs, and the treatment and control of intestinal hookworm (Ancylostoma tubaeforme) and roundworm (Toxocara cati) infections in cats. Revolution is recommended for use in dogs and cats six weeks of age and older." (See "Veterinary Products...selamectin" from Betterchem website provided).

Praziquantel is known to be an antiparasitic (antihelmintic) medication primarily used for the treatment of schistosomiasis (Snail Fever) and fascioliasis (Liver Flukes). It is also used to treat echinococcosis, cysticercosis and intestinal tapeworms. As of 2005 praziquantel is the

primary treatment for human schistosomiasis, for which it is usually effective in a single dose. It is also marketed as a veterinary medicine. (See Wikipedia.com citation for praziquantel).

As such, the art recognizes treatment and prevention of flea and heartworm infections and treatment of tapeworm infections.

**The level of predictability in the art**

The examiner acknowledges the probability and predictability that selamectin and praziquantel would have efficacy in treatment and prevention of fleas and heartworm infections, as well as treatment of tapeworm infections, however the art is silent with regard to the predictability of the formulation have preventative efficacy as asserted for tapeworm.

**The amount of direction provided by the inventor**

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written.

**The existence of working examples**

The working examples set forth in the instant specification are directed to the use of praziquantel and selamectin in various experiments. There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that the formulation as set forth would have the preventative efficacy as asserted.

**The quantity of experimentation needed to make and use the invention based on the content of the disclosure**

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable for prevention of tapeworm. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to prepare, characterize, and test the formulation to determine if indeed the had preventative efficacy as asserted.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determining the scope and contents of the prior art.
Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-4, 6-8, and 10-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey (WO 98/06407) and Lukas et al. (US 2002/0028780), in view of Andrews et al. (US 4,988,696).

Claim 1 is drawn to a formulation comprising selamectin at about 1-16% w/v and praziquantel at about 0.5-10% w/v, together with a carrier, diluent, or adjuvant. Claim 8 provides

praziquantel is present at about 3-9% w/v, and claim 3 provides praziquantel is present at about 6%. Claim 4 provides there is also an ether and optionally a solvent. Claim 6 provides selamectin is provided at around 6-12 mg/kg and praziquantel at up to 18 mg/kg. Claim 7 provides the selamectin is present at about 6-12% w/v. Claim 10 provides that DEGMME or DPGMME is present. Claim 11 provides that a solvent of either ethanol or isopropanol is present. Claim 12 provides for a specific formulation. Claims 13-18 are drawn to methods of treating or preventing flea or heartworm infections, or treating tapeworm infections by administering the formulation of claim 1. Claims 14-17 state the drugs are delivered via the same route, or a different route, and delivered in the same formulation, or in different formulations. Claim 18 provides the method is practiced on a cat. And claim 19 is drawn to a kit comprising selamectin and praziquantel and a carrier. It is noted that the written instructions of claim 19 are of no patentable import to the claim.

Harvey teaches of a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from avermectins and milbemycins, a suitable organic solvent and a carrier. The praziquantel is taught to be present in an amount ranging from 1-10% w/v (see page 2, lines 20-21). Harvey also teaches praziquantel can be combined with any compound of the avermectin group to achieve the purpose of their invention (page 19, lines 19-20). What is not taught is to specifically combine it with selamectin.

Lukas et al. teach an antiparasitic formulation comprising 0.1-50% w/v of an avermectin or milbemycin having endo- or ectoparasitic activity, 1-50% w/v of an ether, optionally an antioxidant, and a solvent (see page 1, column 1). Lukas et al. disclose that the preferred

avermectin in their formulation is selamectin and the preferred ether is DEGMME or DPGMME (see page 1, column 2). Additionally, Lukas et al. teach that the preferred solvent is ethanol or isopropanol (page 2, column 1). Lukas et al. also teach that the antioxidant present can be BHT at a level of less than 0.2% w/v. Lukas et al. teach that their formulations can be prepared for topical or spot-on use, and administered to a dog or cat (page 1, column 2- page 2, column 1). What is not taught is to add praziquantel.

Andrews et al. teach of topical formulations and methods of treating worm diseases by topically applying praziquantel in amounts of from 0.1-5mg/kg body weight (see column 2, lines 25-30).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the active agents, selamectin and praziquantel, to form a single composition with these references before them, and use them in the manner in which they are known to be used in the art, as an anti-helminth. One would have been motivated to combine praziquantel and selamectin in a formulation in the claimed amounts because the agents individually are know to be effective in those amounts. Moreover, one would have been motivated to combine the active agents because it is obvious to combine two compositions each of which is used for the same purpose, to form a new composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. ***In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).*** (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also ***In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960)*** (Claims directed to a method and material for treating cast iron using a mixture

comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and ***Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992)*** (mixture of two known herbicides held prima facie obvious). In the instant case, Harvey teaches it is advantageous to combine two or more anthelmintics with different activity in one composition to obtain a composition having a broad spectrum of activity, and thus reduce the time spent treating the animal and thus reducing the stress on the animal. Andrews et al. and Lukas et al. teach that praziquantel and selamectin can each be delivered topically to animals. Moreover, Andrews et al. states that dermal administration is advantagous, as the animal does not have to be held during treatment, as with injections, nor is there a risk of refusal of medication if administered in a food/orally (see column 2, lines 9-17).One would have been motivated to combine these agents to form a new composition which would be used for the very same purpose. The art teaches both drugs can be administered topically to the dermis, that combination therapy is encouraged to deliver more than one drug at a time, and that dermal application is advantageous due to ease of delivery. The art also teaches the drugs are effective in the concentrations claimed. As such, claims 1, 3-4, 6-8, and 10-19 are seen to be obvious in light of the above references.

## *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Traviss McIntosh
December 14, 2006

12/22/06
Shaojia A. Jiang
Art Unit 1623
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